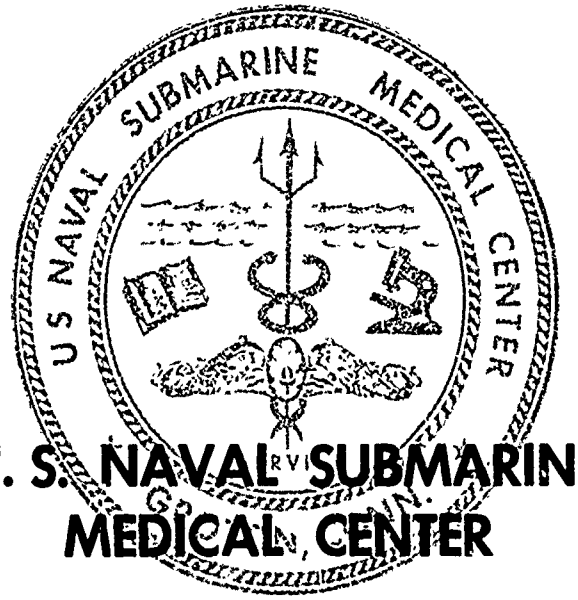

U. S. NAVAL SUBMARINE MEDICAL CENTER

Submarine Base, Groton, Conn.

REPORT NUMBER 655

EFFECT OF 90-DAY EXPOSURE TO 1% CO_2 ON ACID-BASE STATUS OF BLOOD

by

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Bureau of Medicine and Surgery, Navy Department
Research Work Unit MR005.01.01-0125B9XX.01

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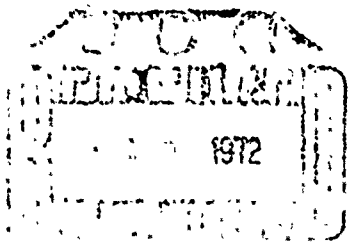

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13 ABSTRACT

Four test subjects were exposed to a 90-day simulated space station environment along with three outside controls. The environmental level of CO_2 was comparable (1% CO_2) to that found in FBM submarines during extended patrols of 60 days' duration.

Frozen anaerobic venous plasma samples were analyzed for pH, P_{CO_2}, HCO_3, Na^+, K^+, and Cl^-. Results similar to those found in submarine exposure showed the existence of a mild respiratory acidosis during days 1-24 of exposure and a compensation of the acidosis during days 25-45 of exposure. A second period of a mild respiratory acidosis developed during the latter days of exposure (46-90 days). All values rapidly returned to normal subsequent to exposure.

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NAVAL SUBMARINE MEDICAL RESEARCH LABORATORY
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SUMMARY PAGE

THE PROBLEM

To determine whether a prolonged exposure to an equivalent of 1% CO_2 in a simulated space-station environment is similar in its effect on the acid-base status of blood as a prolonged exposure in a Fleet Ballistic Missile (FBM) submarine.

FINDINGS

The results of this study showed a mild respiratory acidosis during the first three weeks of exposure followed by a return to control values during the fourth to seventh week of the experiment. The acid-base and electrolyte shifts during this time period are consistent and comparable with data obtained during FBM patrols of seven to eight weeks' duration. As the exposure extended into the eighth week, a mild secondary respiratory acidosis developed. The development of this secondary acidosis was related to a fluctuation that occurred in the CO_2 level of the space-station simulator resulting from difficulties with the solid amine CO_2 scrubber system.

APPLICATIONS

This report will be valuable to those interested in acid-base and electrolyte shifts occurring in long-term, low-level CO_2 exposures in closed environments, such as in undersea habitations or in space stations.

ADMINISTRATIVE INFORMATION

This investigation was conducted as a part of Bureau of Medicine and Surgery Research Work Unit MR005.01.01-0125B9XX-Effect of Exposure to the Total Submarine Atmospheric Environment on Physiological Functions. The present report is No. 1 on this work unit. The manuscript was approved for publication on 2 March 1971 and designated as Naval Submarine Medical Research Laboratory Report Number 655.

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ABSTRACT

Four test subjects were exposed to a 90-day simulated space station environment along with three outside controls. The environmental level of CO_2 was comparable (1% CO_2) to that found in FBM submarines during extended patrols of 60 days' duration.

Frozen anaerobic venous plasma samples were analyzed for pH, P_{CO_2}, HCO_3, Na^+, K^+, and Cl^-. Results similar to those found in submarine exposure showed the existence of a mild respiratory acidosis during days 1 - 24 of exposure and a compensation of the acidosis during days 25 - 45 of exposure. A second period of a mild respiratory acidosis developed during the latter days of exposure (46-90 days). All values rapidly returned to normal subsequent to exposure.

EFFECT OF 90-DAY EXPOSURE TO 1% CO_2 ON ACID-BASE STATUS OF BLOOD OF PERSONNEL IN SUBMARINES AND SPACE STATIONS

INTRODUCTION

Four effects produced by prolonged exposure to low levels of CO_2 have been previously established in a large scale experiment, in which 21 subjects were exposed to 1.5% CO_2 for 42 days. Under these conditions, significant changes have been found in acid-base balance[7], respiratory dead space[5], red cell cation exchange[7], and calcium metabolism[6] in Naval submarine personnel. FBM submarines at the present time are operating at CO_2 levels below 1% CO_2. It was, however, of interest to investigate the effects of long-term exposure if an increased concentration of CO_2 developed during a patrol.

More recent studies carried out on submarines during 60 days' patrol with an exposure of 0.9% and 1.0% CO_2 have shown similar changes in respiratory dead space[3] and calcium metabolism[2]. Evidence of the occurrence of the red cell cation shift resulting in an increase of red cell sodium and decrease of red cell potassium has just been obtained on another patrol study in which the average CO_2 concentration was maintained at 0.9%[1].

The Environmental Physiology Branch of the Naval Submarine Medical Research Laboratory (NSMRL) participated in a 90-day 1% CO_2 exposure study, sponsored by the National Aeronautical and Space Administration for the purpose of comparing results in acid-base parameters in simulated space stations with those obtained on submarines under similar conditions.

MATERIAL AND METHODS

Four test subjects were studied before, during, and after a 90-day exposure in a simulated space station. Three outside control subjects were studied from the 45th day of exposure on to the end of the experiment at the same time intervals as the experimental subjects. The experiment was designed to test a system for recycling materials during long periods in space. The average CO_2 concentration of two recent FBM patrols has been 0.80%[1,3] or 6.1mm Hg P_{CO_2} in 760mm Hg total pressure. The simulated altitude of the chamber in the present experiment was kept at an average of 10,000 feet which equals a total pressure of 521 mm Hg. The CO_2 level was maintained at 5mm Hg P_{CO_2} in 521mm Hg which is an equivalent of 0.96% CO_2. The level of CO_2 throughout the exposure was maintained at similar levels as those existing in an FBM submarine atmosphere during patrol.

Frozen samples of plasma and red cells were sent to NSMRL for analyses of acid-base and electrolyte parameters. The following procedure was used on all samples.

Two vacutainers (Becton, Dickerson and Co.) containing sodium heparin as anticoagulant were used to collect venous blood samples from each subject.

Samples were centrifuged for 15 minutes at 3,000 revolutions per minute. The separated plasma and red cells were quickly aspirated into silicone-greased 5-ml syringes and stored at -20°C until analysis.

Plasma pH and P_{CO_2} were analyzed electrometrically (Instrumentation Laboratory, pH Blood Gas Analyzer Model 113-S1). Plasma pH values were corrected for an alkaline error of +0.03 pH units resulting from centrifugation of the sample at room temperature[9]. Plasma bicarbonate was calculated from an alignment nomogram utilizing plasma pH and P_{CO_2} data. Gasometrically determined bicarbonate, utilizing the Van Slyke manometric technique, was run as a spot check on the accuracy of the bicarbonate data.

For analysis of red blood cell electrolytes aliquots of packed erythrocytes were hemolyzed in distilled water. Direct determinations of Na^+ and K^+ in plasma and the red cell hemolysate were made by flame photometry (Instrumentation Laboratory, Flame Photometer Model 143). Chloride values for both plasma and red cells were obtained by coulometric-amperometric titration using a Buchler-Cotlove Chloridometer^R (Model 4-2008). Correction factors for dilution of the red blood cells were applied and the values calculated as mEq/liter red blood cells.

We found in previous patrol studies[4] that when the plasma is not completely separated from the red cells following centrifugation, an excessive freezing and subsequent thawing results in increased red cell sodium values (25-35 mEq/l). We have discarded such data.

Unfortunately, for the same reason, we found the red cell sodium elevated above the normal range in the blood samples for both the control subjects and the subjects who participated in the experiment reported here. We therefore had to discard all of the red cell data.

Due to external reasons pre-exposure control pH and blood gas data was not available. We have used as control data the blood values obtained after 18 and 25 days post-exposure.

Student's t-test was used as a test of significance for all data.

RESULTS

The time course of the average plasma pH, P_{CO_2} and that of the simulator P_{CO_2} level is presented in Figure 1. The level of simulator CO_2 was maintained relatively constant during the first 38 days of the exposure. However, after 38 days the level of CO_2 rose above 5 mm Hg and fluctuated for the rest of the exposure. This fluctuation was due to difficulties encountered in the operation of the solid amine buffer system which was used for CO_2 absorption. A molecular sieve system was also used during this time period in order to try to stabilize the CO_2 level. The venous pH fell from the first to the tenth day and rose again at the 24th day. The pH then reached a peak after 38 days. There was, however, a relationship between the rise and fall in

pH as the simulator P_{CO_2} fluctuated in the later stages of the exposure (days 45 through 90). Venous P_{CO_2} levels increased slightly during the first few days of the exposure and returned to control levels by the 38th day. As the exposure time was extended, the venous P_{CO_2} then varied directly as the simulator P_{CO_2} level.

The time course of plasma chloride, sodium, and potassium is displayed in Figure 2. Mean plasma chloride and sodium exhibited a tendency to decline during the early exposure period (days 1 to 24) corresponding with the respiratory acidosis (Figure 2). Mean plasma potassium was slightly lowered during the first 31 days of exposure and rose slightly above initial values during the later part of exposure.

Based on the time course of the pH change, we have subdivided the exposure period into three periods: (1) 1-24 days showing the decrease in pH, (2) 25 to 45 days, pH has returned to near control levels, and (3) 46 to 90 days in which a second decline of pH occurs.

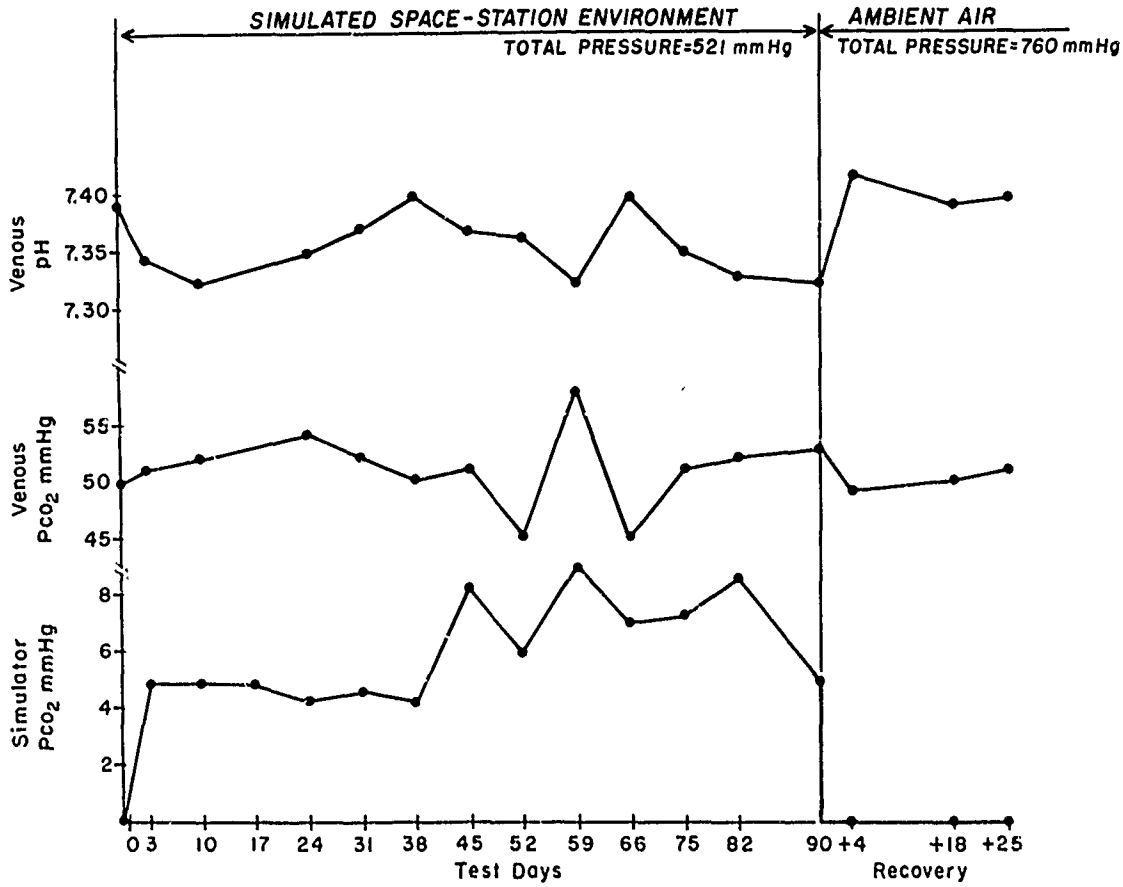

Fig. 1. Time Course of Changes in Plasma pH and P_{CO_2} and of Simulator P_{CO_2} during 1% CO_2 Exposure of 90-Day Duration. Mean values of four subjects.

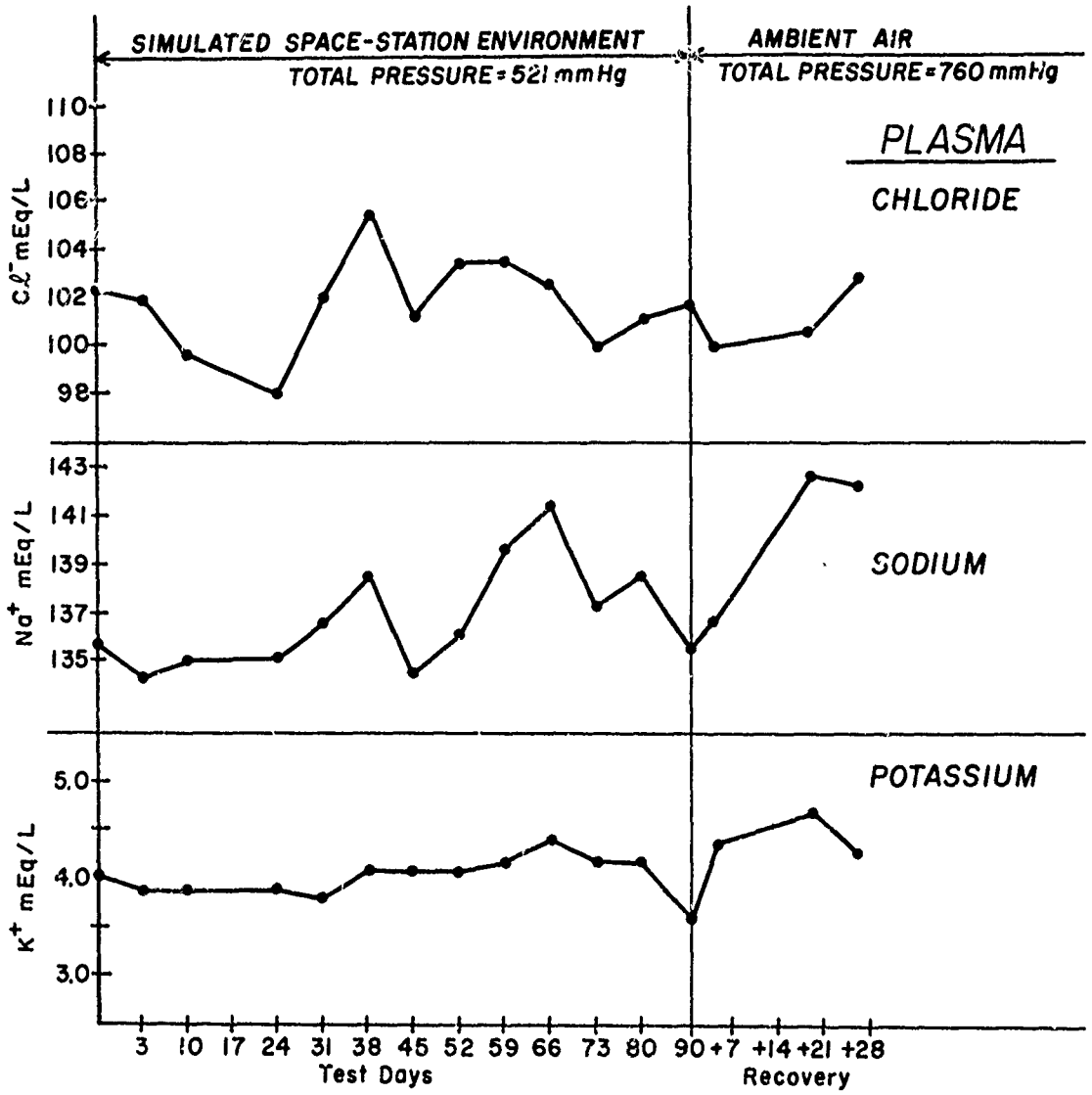

Fig. 2. Time Course of Changes in Plasma Electrolytes During 1% CO_2 Exposure of 90-Day Duration. Mean values of four subjects.

The first two time periods coincided with the phases of uncompensated and compensated respiratory acidosis previously found during prolonged exposure to 1.5% CO_2.[8] For the three control subjects only the periods corresponding to 45 days and from 46 to 90 days were available.

The three control subjects (Table I) did not show any statistical significant change in plasma pH, P_{CO_2}, K^+, and Cl. There was a transitory decrease in plasma sodium at 45 days and of bicarbonate at 46 to 90 days.

The plasma values of the four experimental subjects who were exposed for 90 days to 1.0% CO_2, were grouped as stated above and are shown in Table II. There was a statistically significant decrease in pH during the first 24 days

Table I. Plasma Values of Control Subject (N = 3)

		pH	P_{CO_2} mm Hg	HCO_3 mEq/1	Na^+ mEq/1	K^+ mEq/1	Cl^- mEq/1
Control	Mean	7.378	52.7	29.9	139.8	4.3	100.0
	S.E.M	.010	2.0	1.0	.7	.3	1.2
	N	5	5	5	5	5	5
Corresponding to exposure 1-24 days							
Corresponding to exposure 45 days	Mean	7.339	47.0	27.4	133.8*#	4.0	101.1
	S.E.M	.005	2.2	1.1	.7	.1	.3
	N	3	3	3	3	3	3
Corresponding to exposure of 46-90 days	Mean	7.394	49.4	27.0*#	140.8	4.3	104.1
	S.E.M	.011	1.9	.5	1.4	.1	1.3
	N	14	14	14	14	14	14
Corresponding to Post Exposure 1-25 days	Mean	7.393	53.9	29.6	138.5	4.2	99.7
	S.E.M.	.010	1.4	.6	.7	.2	.6
	N	10	10	10	10	10	10

* Statistically significantly different from controls at the 5% level or better

\# Statistically significantly different from post-exposures at the 5% level and better

Table II. Plasma Values of Experimental Subjects (N = 4)

		pH	P_{CO_2} mm Hg	HCO_3 mEq/1	Na^+ mEq/1	K^+ mEq/1	Cl^- mEq/1
Control	Mean	7.392	50.7	29.8	139.4	4.2	104.2
	S.E.M.	.010	1.9	1.0	5.2	.1	2.8
	N	4	4	4	4	4	4
Exposure 1-24 days	Mean	7.345*#	52.4	27.6*#	135.4#	3.8*#	100.8
	S.E.M.	.009	1.4	.4	.8	.1	.7
	N	12	12	12	16	16	16
25-45 days	Mean	7.379	50.9	29.0	136.6	4.0	102.9
	S.E.M.	.007	1.3	.4	.8	.1	1.0
	N	12	12	12	12	12	12
46-90 days	Mean	7.358	50.2	26.9*#	139.1	4.2	102.2
	S.E.M.	.011	2.4	.4	.9	.1	.8
	N	20	20	20	20	20	20
Post exposure 1-25 days	Mean	7.380	48.2	29.1	139.3	4.2	101.2
	S.E.M.	.009	3.3	.5	1.2	.2	.6
	N	16	16	16	16	16	16

* Statistically significantly different from controls at the 5% level and better

\# Statistically significantly different from post=exposure at the 5% level and better

associated with a fall in plasma potassium. Plasma chloride also declined but the change was not statistically significant. There is a tendency towards another decline of the pH during the exposure period from 46 to 90 days.

The data of the four experimental subjects have also been divided into two parts, those who were on the day watch and those who were on the night watch (Tables II and III). The day watch personnel exhibited a significant decrease

Table III. Plasma Values of Day Watch (N = 2)

		Hct % Vol	pH	P_{CO_2} mm Hg	HCO_3 mEq/1	Na^+ mEq/1	K^+ mEq/1	Cl^- mEq/1
Control	Mean	45.5	7.406	48.2	29.3	1[illegible].2	4.4	107.0
	S.E.M.	1.0	.002	3.6	2.1	8.8	.0	4.8
	N	2	2	2	2	2	2	2
Exposure								
1.24 days	Mean	45.5	7.346*#	53.2	28.0	134.4*#	3.7*#	100.5
	S.E.M.	.6	.007	1.7	.6	1.4	.1	1.5
	N	4	6	6	6	6	6	6
25-45 days	Mean	45.9	7.367*	53.4	29.6	135.6#	4.0	101.4
	S.E.M.	.9	.008	1.5	.7	1.1	.1	1.3
	N	4	6	6	6	4	4	4
46-90 days	Mean	45.9	7.340*#	53.8	27.7	137.0	4.0	100.8*
	S.E.M.	.2	.015	2.9	.5	1.3	.1	.7
	N	8	10	10	10	8	8	8
Post-exposure 1-25 days	Mean	45.0	7.384	45.0	28.8	139.9	4.4	102.0
	S.E.M.	.5	.016	5.9	5.6	1.5	.3	.9
	N	4	8	8	8	6	6	6

* Statistically significantly different from controls at the 5% level and better

\# Statistically significantly different from post-exposure at the 5% level and better

Table IV. Plasma Values of Night Watch (N = 2)

		Hct % Vol	pH	P_{CO_2} mm Hg	HCO_3 mEq/1	Na^+ mEq/1	K^+ mEq/1	Cl^- mEq/1
Control	Mean	46.5	7.378	53.2	30.4	134.5	4.0	101.4
	S.E.M.	1.0	.014	.2	.9	6.0	.2	3.0
	N	2	2	2	2	2	2	2
Exposure								
1.24 days	Mean	45.6	7.328*#	51.6	27.1*	136.4	4.0	101.6
	S.E.M.	1.0	.010	1.2	.7	.7	.1	.9
	N	4	6	6	6	6	6	6
25-45 days	Mean	45.5	7.392	48.4*#	28.5*	137.5	4.0	104.3#
	S.E.M.	.5	.007	1.2	.4	1.2	.1	1.2
	N	4	6	6	6	4	4	4
46-90 days	Mean	44.6	7.376	46.5*#	26.0*#	141.2*	4.3	103.6#
	S.E.M.	.4	.015	2.0	.6	1.0	.1	1.2
	N	8	10	10	10	8	8	8
Post exposure 1-25 days	Mean	44.4	7.377	51.3	29.3	138.8	4.1	100.4
	S.E.M.	.5	.011	.7	.9	1.9	.2	.6
	N	6	8	8	8	6	6	6

* Statistically significantly different from controls at the 5% level and better

\# Statistically significantly different from post-exposure at the 5% level and better

of pH throughout the exposure period and a significant decrease of sodium and potassium during the first 24 days. Plasma chloride decreased after this period, and was statistically significant in the 45 to 90-day exposure period. In the men of the night watch a significant decrease in pH (respiratory acidosis) was limited to the period of 1-24 days, P_{CO_2} was significantly lower during the second and third exposure period. However the limited number of values preclude firm deductions from the data with the limited number of subjects.

DISCUSSION

The results of this study suggest that exposure to 1.0% CO_2 for 90 days causes a mild respiratory acidosis. The respiratory acidosis is most pronounced during the first 24 days. During the period of 25-44 days the respiratory acidosis appears nearly compensated inasmuch as the pH values return practically to the initial levels. This corresponds with previous observations during exposure to 1.5% CO_2[8] as well as with findings obtained subsequently on patrols during which the CO_2 concentration ranged from 0.7% to 0.9% [1,3,5] .

As was seen in Figure 1, the CO_2 level of the simulator varied intermittently during the blood sampling days 45 through 90. Under these conditions, pH varied inversely and P_{CO_2} directly with the cabin CO_2 concentration. There was no respiratory compensation of the mild acidosis during this period. There is also some supportive evidence for this observation in a recent study where a subject was repeatedly exposed to an intermittent level of CO_2, up to 3%, for a period of 6 days. The subject showed no adaptation of blood gas parameters[6].

Throughout the entire exposure period the plasma data from the mean of the night watch showed a definite pattern of lower pH, and chloride, and a higher P_{CO_2} than did the day watch personnel. Since the blood of all test subjects were drawn at the same time, the differences may be related either to diurnal variations, the influence of other variables present in the experimental design, or very possibly the lack of a greater sample size.

It must be emphasized that because of the difficulties inherent in transcontinental shipping of blood samples, and the limited number of subjects, these results must be interpreted with caution. More data should be accumulated preferably with, on site, within chamber, blood gas analysis which is essential when one is measuring subtle changes in blood gases and electrolytes.

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